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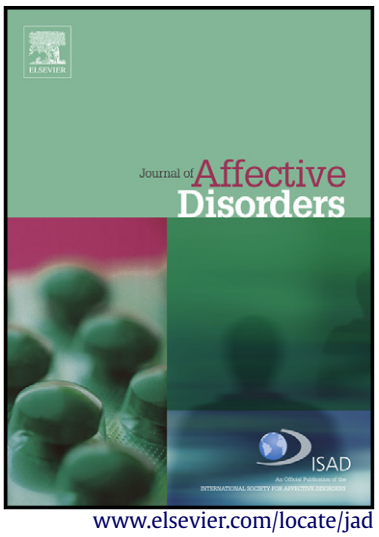

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Health-related physical fitness in patients with bipolar disorder versus healthy controls: an exploratory study

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Abstract

Background: Low physical fitness has been recognized as a prominent behavioral risk factor for cardiovascular diseases and an independent risk factor for all-cause mortality. To date, no studies have systematically assessed physical fitness in patients with bipolar disorder. The aim of the current study was to assess and compare the physical fitness in patients with bipolar disorder against healthy controls.

Methods: Thirty patients with bipolar disorder (16♂, 40.8±11.6 years) and 30 age-, gender- and body mass index (BMI)-matched healthy controls were included. All participants performed the Eurofit test battery and the International Physical Activity Questionnaire. Patients were screened for psychiatric symptoms using the Quick Inventory of Depressive Symptomatology and Hypomania Checklist-32.

Results: Patients with bipolar disorder had a reduced speed of limb movement (15.8±5.7 vs. 11.8±2.2 sec; $p<0.001$), explosive leg muscle strength (134.9±49.0 vs. 167.6±32.3 cm; $p=0.003$) and abdominal muscular endurance (11.5±7.8 vs. 18.3±7.6; $p<0.001$). Backward regression analyses demonstrated that longer illness duration, higher body mass index, higher levels of depression and a lower physical activity level explained the variance in physical fitness.

Limitations: Our data are cross-sectional and cannot establish cause and effect.

Conclusions: The current findings suggest that a lower physical fitness is emerging as an eminent modifiable risk factor for somatic co-morbidity in people with bipolar disorder. In particular less physically active persons, those with a longer illness duration and those with higher levels of depression might benefit from specific rehabilitation interventions aimed at increasing physical fitness.

Keywords: physical fitness; physical activity; bipolar disorder

1. Introduction

Increased rates of cardio-vascular diseases (CVD) (Goldstein et al., 2009; Prieto et al., 2014) and associated premature mortality (Fiedorowicz et al., 2014) have recently become a major concern in patients with bipolar disorder. Underlying reasons for the development of CVD in patients with bipolar disorder are complex and consist of genetic risk (Ellingrod et al., 2012), cardio-metabolic side-effects of antipsychotic treatment (Vancampfort et al., 2013) and an unhealthy lifestyle (Cerimele and Katon, 2013). Unhealthy lifestyle factors include a sedentary lifestyle (Janney et al., 2014), higher prevalence of smoking, and high rates of substance abuse (Waxmonsky et al., 2005). To compound this, patients with bipolar disorder have limited access to general somatic health care (Mitchell et al., 2009; De Hert et al., 2011).

In the general population low physical fitness is established as a prominent risk factor for CVD and an independent risk factor for all-cause mortality (Wei et al., 1999). Physical fitness can be defined as a set of independent attributes that are related to the ability to perform physical activities. Some of these components (including cardio-respiratory fitness, muscular endurance, muscular strength and flexibility) are more closely related to health, while others (such as coordination and whole body balance) are more related to performance (Pate, 1998).

To date, research on the physical fitness in patients with bipolar disorder is lacking. In addition, it still needs to be established if and to what extent the recently observed lack of physical activity participation in patients with bipolar disorder (Janney et al., 2014; Vancampfort et al., 2013b) is associated with a reduced health and performance related physical fitness. Identifying which health and performance related physical fitness components are impaired in patients with bipolar disorder, may assist in developing physical rehabilitation strategies to prevent or reduce the increased risk for somatic co-morbidities.

Research is required to investigate the physical fitness of patients with bipolar disorder to disentangle these relationships.

The primary objective of this study therefore was to examine differences in health and performance related physical fitness between patients with bipolar disorder and healthy controls matched for age, gender and body mass index (BMI). Secondary objectives were to assess associations of physical fitness components and physical activity levels and psychiatric symptoms.

2. Methods

2.1. Participants and procedure

Over a 6-month period, inpatients with a DSM-V diagnosis of bipolar disorder (American Psychiatric Association, 2013) of the UPC KU Leuven campus Kortenberg in Belgium were invited to participate. Since severe substance abuse might impair the physical fitness test performances (Herbsleb et al., 2013), participants were excluded if they had a co-morbid DSM-V diagnosis of substance abuse during the previous 6 months. The somatic exclusion criteria included evidence of significant cardiovascular, neuromuscular and endocrine disorders which, according to the American College of Sports Medicine (2013), might prevent safe participation in the study. All participants received a physical examination and baseline electrocardiogram before testing. Healthy control subjects were recruited among the personnel of the participating centers. All control subjects were volunteers who received a general physical examination in the previous year and reported to be free of significant cardiovascular, neuromuscular and endocrine disorders that might hinder safe participation (16). An independent statistician blinded for the physical activity and physical fitness outcomes performed the matching for age, gender and body mass index (BMI). All

participants completed the International Physical Activity Questionnaire (Craig et al., 2003) and performed the Eurofit test battery (Oja and Tuxworth, 1995). Participants were requested to refrain from eating, drinking coffee or smoking during a two-hour period prior to the tests. Participants with bipolar disorder additionally completed the Quick Inventory of Depressive Symptomatology self-report (Rush et al., 2003) and the Hypomania Checklist-32 (Angst et al., 2005).

The study procedure was approved by the Scientific and Ethical Committee of the UPC KU Leuven, campus Kortenberg, Belgium and conducted in accordance with the principles of the Declaration of Helsinki. All participants gave their informed written consent. There was no compensation for participation in the study.

2.2. The Eurofit test battery

Supervision and measurement of the Eurofit test battery (Oja and Tuxworth, 1995) was performed by one trained mental health physical therapist. The Eurofit test battery included the assessment of the following measures: whole body balance, speed of limb movement, flexibility, explosive strength, static strength, abdominal muscular endurance and running speed. The procedure has been described more in detail elsewhere (Vancampfort et al., 2012a).

2.3. International Physical Activity Questionnaire (IPAQ) - long version

A structured format (Craig et al., 2003) that asked participants to recall activities for each of the last seven preceding days in morning, afternoon, and evening time periods was used. On the basis of what activities participants self-reported, the interviewer clarified the perceived intensity of that specific activity. A continuous indicator was calculated as a sum of weekly metabolic equivalent (MET)-minutes per week of physical activity. The MET energy

expenditure was estimated by weighting the reported minutes per week within each activity category by a MET energy expenditure estimate assigned to each category of activity. The weighted MET-minutes per week were calculated as duration x frequency per week x MET intensity, which were then summed across activity domains to produce a weighted estimate of total physical activity from all reported activities per week.

2.4. Smoking behavior

Participants were asked whether they smoked or not, and if so, how many cigarettes they smoke per day on average.

2.5. Quick Inventory of Depressive Symptomatology self-report (QIDS -SR)

QIDS-SR (Rush et al., 2003) consists of 16 items each ranging from 0 to 3. Scores range from 0 to 27 with higher scores indicative for higher symptom severity. The QIDS-SR is a standardized measure of depressive symptoms and has demonstrated adequate psychometric validity in patients with bipolar disorder (Trivedi et al., 2004).

2.6. Hypomania Checklist - 32

The HCL-32 (Angst et al., 2005) consists of 32 yes/no statements regarding a period when the patient remembers he was in a "high" mood. Items ask whether specific behaviors (e.g., "I spend more money/too much money"), thoughts (e.g., "I think faster"), or emotions (e.g., "my mood is significantly better") were present in such a state. Scores range from 0 to 32. Higher scores reflect more severe hypomanic states. The HCL-32 has been cross-culturally validated; also in a Belgian subsample (Angst et al., 2010).

2.7. Anthropometric measurements

Body weight was measured in light clothing to the nearest 0.1kg using a SECA beam balance scale, and height to the nearest 0.1cm using a wall-mounted stadiometer.

2.8. Medication use

We recorded the use of antipsychotic medication, antidepressants, mood stabilizers, benzodiazepines, anti-cholinergic, and somatic medication. Antipsychotic medication was recorded and converted into a daily equivalent dosage of chlorpromazine according to the consensus of Gardner et al. (2010). Mean dosages of specific mood stabilizers and antidepressants were reported when they were used by at least 10 participants.

2.9. Statistical analyses

Data were assessed for normality using the Shapiro-Wilk test and found to have a normal distribution. Descriptive statistics are therefore presented as mean ± standard deviation (SD). Unpaired t-tests with post-hoc Bonferroni correction for continuous variables and Fisher exact tests for categorical variables (gender) ($p<0.05$) were used to examine differences in characteristics between patients and healthy controls. Relationships between variables were calculated when data were available for all participants by using Pearson correlation coefficients. In order to correct for multiple testing, correlation coefficients are considered significant when $p<0.01$. Backward stepwise regression analyses were performed to evaluate independent variables explaining the variance in Eurofit test item performances. To prevent overfitting of the models, only variables significant in the univariate analyses were entered into the final model. To test for multicollinearity, a variance inflation factor (VIF) was computed for each independent variable in the model. Values above 3 were used to indicate a

multicollinearity problem in the model (Kleinbaum et al., 2013). If we encountered a VIF above 3 between two independent variables, we only included the independent variable with the strongest correlation coefficient with the dependent variable. Statistical analyses were performed using the statistical package SPSS version 22.0 (SPSS Inc., Chicago, IL).

3. Results

3.1. Participants

A total of 44 inpatients with bipolar disorder were initially screened. Six persons with co-morbid substance abuse during the previous 6 months were excluded. Two persons were excluded as a consequence of a cardiovascular or neuromuscular disorder that might prevent safe participation. Of the 36 eligible persons with bipolar disorder, 6 declined to participate (i.e., were not interested). All eligible 30 enrolled patients with bipolar disorder completed the study and there were no dropouts. Thirty healthy controls matched for age, BMI and gender filled out the IPAQ and completed the Eurofit test battery. Participants' characteristics for both groups are shown in Table 1. Forty percent (n=12) of the patients with bipolar disorder smoked compared to 23.3% (n=7) of the healthy controls (p=0.17).

[Insert Table 1 about here]

Mean duration of illness was 15.2±10.3 years. An overview of the medication use is presented in Table 2. Mean daily equivalent dosage of chlorpromazine was 504.7±315.2mg/day (n=29) and the mean dose of lithium (n=10) was 985.0±601.4mg/day. The mean QIDS-SR and HCL-32 score were respectively 6.8±4.5 and 15.1±6.3.

[Insert Table 2 about here]

3.2. Differences in health and performance related physical fitness and physical activity between participants with bipolar disorder and healthy controls

Health and performance related physical fitness variables of both groups are presented in Table 3. Patients with bipolar disorder demonstrated an impaired speed of limb movement, explosive muscle strength and abdominal muscle endurance compared with age-, gender- and BMI-matched healthy controls (all $p<0.0056$). There was a trend ($p<0.10$) for a reduced flexibility, handgrip strength and running speed. Apart from these differences in health and performance related physical fitness, patients with bipolar disorder were significantly less physically active than healthy controls: 1482.2±1132.8 versus 2481.1±1470.7 MET-minutes per week ($p=0.005$).

[Insert Table 3 about here]

3.3. Associations with Eurofit test item performances in patients with bipolar disorder

Table 4 shows the correlations between demographical and clinical variables (if data were available for the entire sample) and health and performance related physical fitness. All significant variables were included in the backward stepwise regression analyses. In those regressions where age and illness duration were both included the VIF was above 3 for both variables, which was an indication for multicollinearity. In these cases, we included only the variable with the highest correlation coefficient (i.e., illness duration in all cases). Parameter estimates, standardized and unstandardized coefficients, standard error of measurements and significance levels of all backward stepwise regression models are presented as online only supplementary material (Appendix 1).

[Insert Table 4 about here]

The backward stepwise regression analyses showed that the variance in illness duration and the level of depression could explain 47.4% of the variance in whole body

balance and 39% of the variance in running speed. In the same way, 68.7% of the variance in speed of limb movement and 49.5% of the variance in explosive muscle strength can be explained by the variance in illness duration and the level of physical activity participation. Exactly 19% of the variance in handgrip strength was explained by the variance in depression. Finally, 31.4% of the variance in flexibility was explained by the variance in illness duration and BMI, while 56.5% the variance in abdominal muscle endurance was explained by the variance in illness duration, BMI and the level of depression.

4. Discussion

4.1. General findings

To our knowledge, the present study is the first to compare health and performance related physical fitness in inpatients with bipolar disorder with age, gender and BMI matched healthy controls. Our data demonstrate that inpatients with bipolar disorder have an impaired health and performance related physical fitness. The present findings are also the first to indicate lower levels of physical activity are an important contributing factor to the reduced health and performance related physical fitness in patients with bipolar disorder. Also a longer illness duration proved to be a strong predictor correlate for the performance on several Eurofit test items. Of interest is that longer illness duration appears a more important determinant of physical fitness than biological age. Previous research already demonstrated that illness duration rather than biological age contributes, especially in the early stages of the disease, to the accumulation of medical illnesses (Soreca et al., 2008). Possible reasons include the cumulative long-term effect of poor health behaviors such as physical inactivity, but also a longer lifetime exposure to depressive symptoms may translate into a poorer physical fitness. It might be speculated that those who are depressed are less likely to engage in physical activity which on its turn might result in a lower health and performance related physical fitness (Vancampfort et al., unpublished results). A third possible mechanism might be that a

low self-efficacy and negative outcome expectations patients with depressive feelings are often confronted with when performing physical fitness tests, result in a worse test performance (Krämer et al., 2014). Fourth, also the low-grade inflammation associated with the manifestation of depressive symptoms (Leboyer et al., 2012) should be tested more in detail. Inflammatory processes may cause pathological microvascular changes that can affect gas transfer across the alveolar-capillary membrane, which in turn may affect the circulatory, respiratory, and muscular systems involved in supplying oxygen to the body (Ostermann et al., 2013). Fifth, bipolar disorder is uniquely characterized by instability, fluctuations, course variability and unpredictability, ongoing symptoms and ongoing fluctuations during the remitted phase, disruption of circadian rhythms that may all be part of a common diathesis that may lead to medical disorders and a reduced ability to perform daily life activities (Frank et al., 2000). Finally, and in accordance with previous research in patients with schizophrenia (Vancampfort et al., 2012a) the variance in BMI explained the variance in the Eurofit test performance, especially in those physical fitness tests requiring propulsion or lifting of the body mass (i.e., sit-ups and sit-and research test).

4.2. Clinical relevance

Our data indicate that increasing health and performance related physical fitness and physical activity participation should be key targets in the multidisciplinary treatment of patients with bipolar disorder. Patients with a longer illness duration and depressive symptoms may be particularly affected and need additional support. This is of importance for the majority of patients since depression pre-dominates the clinical picture of bipolar disorder (American Psychiatric Association, 2013), and non-response to treatment is highly prevalent resulting in residual depressive symptoms (Fekadu et al., 2009). Secondly, our data also indicate that lifestyle interventions should not only consider cardio-respiratory fitness but also

other health and performance related physical fitness components including muscular endurance and muscular strength. The current findings therefore suggest a potential role in support for the promotion of resistance training in addition to aerobic fitness training as part of physical activity recommendations. Due to the lack of physical activity and physical fitness research in patients with bipolar disorder there are currently no detailed physical activity recommendations available for this clinical population. Until such recommendations are made available and since a substantial amount of inpatients with bipolar disorder are taking antipsychotic medication (in our sample: 29/30), they should at a minimum comply with the physical activity recommendations for those taking antipsychotic medication (Vancampfort et al., 2012b).

4.3. Study limitations

Present findings need to be interpreted with caution because of some methodological limitations. Firstly, this was a study in volunteers, and hence our data may overestimate health and performance related physical fitness and physical activity participation in patients with bipolar disorders and in healthy controls. Nevertheless, there was a good response rate in the bipolar disorder group which should prevent serious distortion of the results due to selection bias. In the healthy controls' group physical activity scores were in agreement with several other Belgian studies (Philippaerts et al., 1999; De Cocker et al., 2009). This way a selection bias in favor of healthier control volunteers cannot be excluded. Another important limitation was the reliance on self-reported recall physical activity, a method that is prone to both systematic and random errors (Soundy et al., 2014). Thirdly, our data are cross-sectional and cannot establish cause and effect nor can directionality between the variables be deduced with certainty. Although increased physical activity participation would improve health and performance related physical fitness, it is also plausible that those with a more beneficial

health and performance related physical fitness would tend to be more physically active. So, it was impossible to ascertain if more favorable health and performance related physical fitness was due to or rather the consequence of more physical activity. Longitudinal prospective studies and intervention studies are needed to clarify whether improvements in health and performance related physical fitness are due to participation in physical activity.

In conclusion, the current study shows that inpatients with bipolar disorder are less physically fit than a matched control group. Therefore, a lower physical fitness emerges as an eminent modifiable risk factor for somatic co-morbidity in patients with bipolar disorder. In particular less physically active persons, those with a longer illness duration and those with depression might benefit from specific rehabilitation interventions aimed at increasing physical fitness.

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Table 1.

Comparisons in baseline characteristics between persons with bipolar disorder and healthy controls

Variables	**Bipolar disorder (n=30)**	**Healthy controls (n=30)**	**p**
Gender (M/F)	16/14	16/14	1.0
Age (years)	40.8±11.6	40.5±10.8	0.67
BMI (kg/m²)	26.1±3.5	26.4±4.1	0.49
Smoking° (cig/day)	21.7±16.4	14.1±7.9	0.19

Data expressed as mean ± standard deviation, BMI = body mass index, QIDS=Quick Inventory of Depressive Symptomatology, HCL-32= Hypomanic Checklist – 32, °only those who smoke were included: 12 persons with bipolar disorder and 7 healthy controls, *significant after Bonferroni-correction ($p<0.0056$).

Table 2.

Medication use among people with bipolar disorder (n=30) screened prior to participation

Type of medication	n prescriptions
Antidepressants	8
Escilatopram	1
Sertraline	3
Trazodone	3
Venlafaxine	1
Mood stabilizers	21
Valproic acid	9
Lithium carbonate	10
Lamotrigin	2
Antipsychotic medication	29
Amisulpride	4
Aripiprazol	5
Clozapine	2
Olanzapine	9
Paliperidone	1
Quetiapine	10
Risperidone	1
Other medication	28
Benzodiazepine	19
Somatic medication	9

Table 3.

Eurofit test performance of the study participants

Fitness components	**Eurofit test - items**	**Bipolar disorder (n=30)**	**Healthy controls (n=30)**	**p**
Whole body balance	FBA (n/30sec)	13.8±8.0	10.9±7.2	0.14
Speed of limb movement	PLT (sec)	15.8±5.7	11.8±2.2	<0.001*
Flexibility	SAR (cm)	19.8±11.1	24.4±8.1	0.07
Explosive muscle strength	SBJ (cm)	134.9±49.0	167.6±32.3	0.003*
Handgrip strength	HGR (kg)	38.6±11.4	46.6±12.4	0.011
Abdominal muscle endurance	SUP (number/30sec)	11.5±7.8	18.3±7.6	0.001*
Running speed	SHR (sec)	27.1±7.6	23.9±4.0	0.049

*significant after Bonferroni-correction ($p<0.0056$), FBA=flamingo balance, PLT= plate tapping, SAR= sit-and-reach, SBJ=standing broad jump, HGR= handgrip strength, SUP=sit-ups, SHR=shuttle run, NS= not significant.

Table 4.

Associations between physical fitness, physical activity and demographical and clinical characteristics in bipolar disorder (n=30)

	FBA	PLT	SAR	SBJ	HGR	SUP	SHR
Age (yrs)	0.26	0.55*	-0.41	-0.39	-0.10	-0.57*	0.33
Illness duration (yrs)	0.54*	0.79**	-0.60**	-0.60**	-0.23	-0.62**	0.55*
BMI (kg/m²)	0.47*	0.09	-0.49*	-0.33	0.019	-0.48*	0.32
QIDS-SR score	0.59*	0.40	-0.36	-0.55*	-0.47*	-0.56*	0.49*
HCL-32 score	-0.05	-0.10	-0.27	0.21	0.41	-0.10	-0.29
IPAQ total MET	-0.55*	-0.51*	0.14	0.56*	0.42	0.56*	-0.44

*p<0.01, **p<0.001, °derived from the International Physical Activity Questionnaire, FBA=flamingo balance, PLT= plate tapping, SAR= sit-and-reach, SBJ=standing broad jump, HGR= handgrip strength, SUP=sit-ups, SHR=shuttle run, BMI=body mass index, QIDS=Quick Inventory of Depressive Symptomatology, HCL-32= Hypomanic Checklist – 32, IPAQ= International Physical Activity Questionnaire, AP= antipsychotic medication expressed as chlorpromazine equivalent.

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Conflicts of interest
None.

Contributors
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